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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, DC 20460

FEB 9 – 1989

OFFICE OF
PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Registration No. 1471-101 (DEB No. 4587) - Tebuthiuron on Rangelands and Pastures - Protocol for Magnitude of Residues Studies for Tebuthiuron Reregistration (No Accession Number)

FROM: Nancy Dodd, Chemist
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TO: Robert J. Taylor, PM 25
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and

Toxicology Branch II
Herbicide, Fungicide, and Antimicrobial Support
Health Effects Division (TS-769C)

THRU: Richard D. Schmitt, Ph.D., Acting Chief
Dietary Exposure Branch
Health Effects Division (TS-769C)

## Introduction

Elanco Products Company submits a letter dated October 25, 1988, a copy of a presentation made to EPA in a meeting on September 27, 1988, data on usage and sales of tebuthiuron, and a proposed protocol for determining the magnitude of residues of tebuthiuron in forage and hay following application to rangelands and pastures. The present submission and protocol primarily concern the field studies on pastures and rangelands which are needed to provide residue data for tebuthiuron on fresh grass and field-dried hay. Label changes which Dietary Exposure Branch (DEB) previously requested are also discussed. The present submission is a response to the Tebuthiuron Registration Standard dated

July 1987 and DEB's reviews dated December 10, 1987 (N. Dodd) and August 12, 1988 (M. Kovacs). Previously submitted residue data protocols were found to be inadequate.

Summary of Deficiencies That Still Need Resolution (See also the DEB Chapter dated February 27, 1987 of the Tebuthiuron Registration Standard)

1. Nature of the residue in animals;

2. Data from FDA multiresidue protocols;

3. Storage stability data;

4. Data depicting tebuthiuron residues of concern in or on fresh grass and field-dried hay of predominant grasses for various areas, but to include at least one site for each of the following grasses: Bermuda grass, bluegrass, and bromegrass or fescue; and

5. Magnitude of the residue in meat, milk, poultry, and eggs.

6. The submitted analytical method utilizing gas chromatograpy with a flame photometric detector is adequate to generate residue data for tebuthiuron in or on grass and grass hay including its metabolites 103(OH), 104, and 109. If the minor metabolites 104(OH), 106, 107, and 108 are determined by Toxicology Branch (TB) to be of toxicological concern, they would also have to be analyzed by a validated method.

Conclusions

A. Conclusions relating to the nature of the residues in animals, FDA multiresidue protocols, storage stability, and magnitude of the residue in meat, milk, poultry, and eggs as outlined in the DEB Chapter of the Tebuthiuron Registration Standard of February 27, 1987 were not addressed in the present submission.

B. The conclusions regarding the present submission are as follows:

2a. There is no assurance that all rangelands are fenced and/or small enough for convenient livestock removal. Grazing and hay restrictions for all rangelands are not practical.

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2b. The requirement for aerial applications is not waived for these pellet formulations, Spike 20P and 40P (see also DEB's conclusion re: Deficiency No. 2b under "Detailed Considerations" that follows in this review).

2c. The petitioner has agreed to revise the Spike 20P and 40P labels to restrict applications to one per year.

2d. The petitioner has agreed to revise the Spike 40P label by deleting the statement "Do not broadcast Spike 40P on pastureland."

3a. The eight States proposed by the petitioner to obtain residue data (Texas, Oklahoma, Missouri or Kansas, Utah, Arkansas, Iowa, Ohio, and New Mexico or Arizona) will not be adequate for nationwide use.

3b. The petitioner's proposal to use the major grass species in the proposed test locations, with at least one test site for each of the representative grass species (fescue/bromegrass, bluegrass, and Bermuda grass) is acceptable.

3c(1). The petitioner's use of Spike 20P on the rangeland sites and Spike 40P on the pastureland sites is acceptable. The total test sites should, however, involve at least 16 States.

3c(2). Aerial applications will be needed for these pellet formulations.

3c(3) / 3c(4). The 4 lb ai/A rate would be adequate for all residue studies on rangeland and pastureland provided the Spike 40P label is revised so that the maximum broadcast rate for pastureland/ rangeland is 4 lb ai/A. Individual plant treatments are needed unless the petitioner removes directions for individual plant treatments from the label.

4. The Spike 20P and 40P labels should be revised by addition of the statement:

> "However, do not graze livestock within 1 year of application."

5. The petitioner's proposals that initial forage sampling be delayed until at least 0.5 inch of

rain has fallen and that sampling be suspended during dormancy may not be valid for all cases (see also Frequency of Forage Sampling that follows in this review). The objective of the residue data test is to know the maximum residue level that may occur on grasses at any time following applications.

6. The petitioner's proposals that hay sampling begin 1 year after application and that samples be collected 2 to 4 times between 1 and 2 years after application are acceptable.

7. Natural existing rangeland/pastureland sites should be used. Additionally, some irrigated pasture tests would be appropriate in the areas where irrigation is used. Areas which would not normally be irrigated should not be irrigated.

Recommendations

1. DEB recommends that a copy of this review be sent to the registrant.

2. DEB recommends that the deficiencies cited under "Summary of Deficiencies that Still Need Resolution" be addressed by the registrant.

3. The petitioner should address the deficiencies listed in Conclusions 2a, 2b, 2c, 2d, 3a, 3c(1), 3c(2), 3c(3)/ 3c(4), 4, and 5 (under B above).

## DETAILED CONSIDERATIONS

Deficiencies which were discussed in DEB's August 12, 1988 review (M. Kovacs) are restated below, followed by the petitioner's responses and DEB's conclusions.

Deficiency 2a

The Spike 20P and 40P labels should be amended. Grazing and hay restrictions should be applicable to pasture uses only; these restrictions are not practical for proposed rangeland applications; therefore, the Spike 20P label should be revised accordingly.

Petitioner's Response to Deficiency 2a

Rangelands are fenced so that livestock can be removed from a grazing area.

DEB's Conclusion re: Deficiency 2a

There is no assurance that all rangelands are fenced and/or small enough for convenient livestock removal. Therefore, grazing and hay restrictions for all rangelands are not practical.

Deficiency 2a is not resolved.

Deficiency 2b

If intended by the registrant, the Spike 20P and 40P labels should be amended to restrict use to ground applications only for Spike 20P (pastures and rangelands) and Spike 40P (pastureland).

Petitioner's Response to Deficiency 2b

The petitioner requests a waiver of the requirement for aerial applications. The formulations to be used are pellets which can be evenly distributed with the appropriate equipment regardless of whether the application is by ground or air. Tebuthiuron pellets are dissolved by rain and tebuthiuron is then taken up by roots of plants. No foliar surface residues are involved.

DEB's Conclusion re: Deficiency 2b

There is no assurance as to what ground and aerial equipment will be used by the many growers. It would seem that tebuthiuron applications to large rangelands by aerial means would be more appropriate especially for those rangelands containing hillsides and rough terrain. Therefore, the requirement for aerial applications is not waived for these pellet formulations Spike 20P and Spike 40P.

Deficiency 2b is not resolved.

Deficiency 2c

Restrict application on the Spike 20P and 40P labels to one application per year.

Petitioner's Response to Deficiency 2c

Elanco will revise the Spike 20P and 40P labels to restrict applications to one per year.

DEB's Conclusion re: Deficiency 2c

Deficiency 2c will be resolved upon receipt of the revised labels.

Deficiency 2d

If intended by the registrant, delete the restriction against broadcast application of Spike 40P to pastureland.

Petitioner's Response to Deficiency 2d

Elanco will revise the Spike 40P label to delete the restriction against broadcast application of Spike 40P to pastureland.

DEB's Conclusion re: Deficiency 2d

Deficiency 2d will be resolved upon receipt of a revised label for Spike 40P, which has been revised by deletion of the statement "Do not broadcast Spike 40P on pastureland."

Deficiency 3a

In the residue data protocol, the number or specific State locations of the intended "study sites" have not been identified in each of the four regions to be tested. DEB recommends study sites should be located in the following States: Northeast region (New York, Pennsylvania), North Central region (Kansas, Missouri, Oklahoma, Nebraska, North Dakota, South Dakota), Southeast region (Kentucky, Tennessee, Arkansas, Texas, Virginia) and Western region (Colorado, Oregon, Wyoming).

Petitioner's Response to Deficiency 3a

The Registration Standard requests residue trials be conducted in 16 States (Appendix C). Eight (8) of the requested 16 States each represent 1 percent or less of the total tebuthiuron used on rangeland/pastureland. The Agency selection of 16 States was based on production of domestic and wild hay in the United States. Areas treated with Spike for brush control however, are not amenable to haying operations since the dead standing brush would interfere with such operations. The grasses in such areas are "harvested" by grazing animals. Hence, the criteria used by the Agency for selecting the States for residue studies are not appropriate for a rangeland/pastureland brush control chemical such as tebuthiuron.

Elanco proposes to conduct studies in eight (8) States--Texas, Oklahoma, Missouri or Kansas, Utah, Arkansas, Iowa, Ohio, and New Mexico or Arizona. These States have been selected based on the current usage of tebuthiuron for rangeland and pastures. Tebuthiuron has been registered for use

on rangeland since 1979 and on pastureland since 1983. Sales have been basically flat in these markets the past several years. If expansion of product usage is to occur, it is anticipated to be within the States where significant sales exist today. There are certain areas of the United States, such as the Northeast, where there is no rangeland and where no significant sales of tebuthiuron for pastureland are ever anticipated.

The studies in Texas, Oklahoma, Utah, and New Mexico or Arizona would be on rangeland. The studies in the remaining four States would be on pasture. Tebuthiuron usage per year on pastures/rangeland is listed below:

| State | % of Total lbs ai |
|---|---|
| [redacted] | |

The percent of total sales of tebuthiuron for rangeland and pastureland is listed below for the States for which EPA has requested residue data:

| State | Percent of Total Sales |
|---|---|
| [redacted] | |

COMMERCIAL/FINANCIAL INFORMATION IS NOT INCLUDED

DEB's Discussion/Conclusion re: Deficiency 3a

Originally, the petitioner argued for the use of tebuthiuron in controlling brush on rangeland in only two States, Texas and Oklahoma. In June 1980, he argued to extend the use to the States of Arizona, New Mexico, and Kansas. The petitioner now has a Section B that allows use of tebuthiuron on grasses all over the United States. The petitioner argues, however, that he wants to generate residue data in only 8 States (Texas, Oklahoma, Missouri or Kansas, Utah, Arkansas, New Mexico or Arizona, Iowa, and Ohio) instead of the 16 States recommended by the Tebuthiuron Registration Standard because his sales (which DEB does not have authentic records of) are good in those 8 chosen States and basically flat in the other 8 States mentioned in the Tebuthiuron Registration Standard. If a pesticide is registered for use all over the United States, it is not feasible to base the collection of residue data on the company's present-day sales; they can change. For example, tebuthiuron use was once limited to only two States, Texas and Oklahoma.

The production of grasses involves all parts of the United States. Climatic conditions divide the United States into five major pasture regions, as shown below (see also Fourth Edition Crop Production, R.J. Deloret, L.J. Greub, H.L. Ahlgren, Prentice-Hall, Inc., Englewood Cliffs, N.J., 1974):

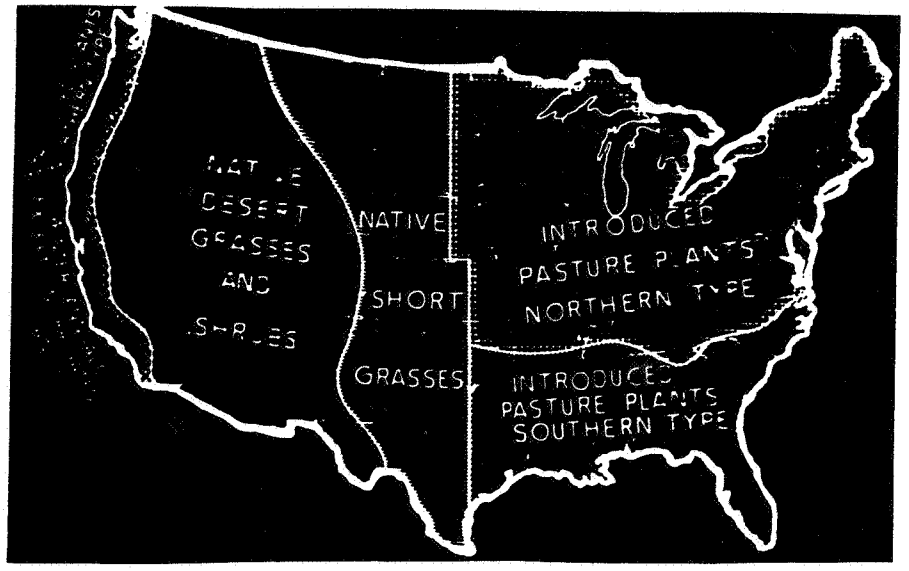



Figure 1. The five pasture regions of the United States (Courtesy U.S.D.A.)

Section 180.34(f)(9)(xvii) of Title 40 of the Code of Federal Regulations (40 CFR 180.34(f)(9)(xvii) Grass forage, fodder, and hay group stipulates that residue data may be generated on the representative commodities Bermuda grass,

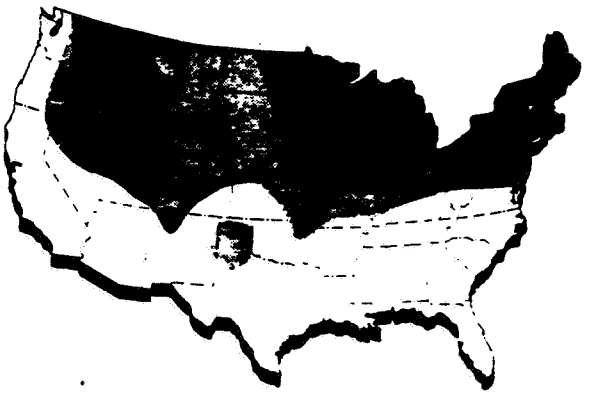
bluegrass, and bromegrass or fescue. The following three maps show the major growing areas for bromegrass, Kentucky bluegrass, and Bermuda grass. Residue data on these three grasses would practically cover all geographical areas of the United States. In view of the preceding, the following residue data requirement as specified in the February 27, 1987 Dietary Exposure Chapter of the Tebuthiuron Registration Standard is geographically appropriate and reasonable since it would involve only 16 test sites for such a major crop:

- Data depicting tebuthiuron residues of concern in or on fresh grass and field-dried hay of Bermuda grass, bluegrass, and bromegrass or fescue treated with a single application of a P/T formulation, by ground or air equipment, at 4 lb ai/A. Fresh grass samples must be collected every 2 weeks for the first 3 months following application, and monthly for the following 21 months in order to determine the maximum residue level that may occur at any time following application. Hay samples must be collected up to 2 years following the application. If other grasses are tested, the grass species must be identified for each test and the species must be representative for the region in which it was tested. Tests must be conducted in Arkansas (3%), Kansas (4%), Kentucky (6%), Missouri (11%), New York (5%), Oklahoma (4%), Pennsylvania (4%), Tennessee (4%), Texas (13%), and Virginia (3%), which collectively produced ca. 57 percent of the total domestic hay crop in 1982 (production figures follow in parentheses). Tests must also be conducted in Colorado (3%), Nebraska (16%), North Dakota (10%), Oregon (4%), South Dakota (12%), Texas (2%), and Wyoming (5%), which together with Kansas (8%) and Oklahoma (5%), collectively produced ca. 65 percent of the total 1982 wild hay crop (and thus represent rangeland grasses). The combined tests will adequately represent the major rangeland and pasture regions of the United States (production figures were obtained from the 1982 Census of Agriculture, Vol. 1, Part 50, p. 330).

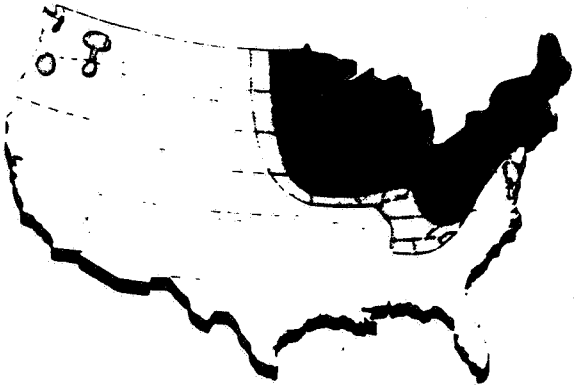
Deficiency 3a has not been resolved.

Deficiency 3b

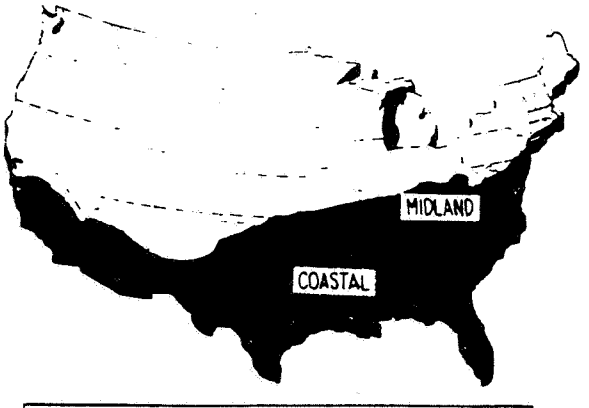
In the residue data protocol, the representative grass species tested at each study site was not adequately representative of the region in which it was tested. In the resubmitted protocols, the representative grass species tested at each study site (i.e., fescue/bromegrass, bluegrass, Bermuda grass) must be identified and the species must be representative for the region in which tested.



Areas of major use and distribution of smooth bromegrass



Kentucky bluegrass is present in all states of the U.S., including Alaska, but is most important agriculturally in the north central and northeastern sections. It is important as a seed crop in parts of Idaho, Washington, and Oregon.




Bermudagrass growing areas in the U.S.

Figure 2. Major growing areas for bromegrass, Kentucky bluegrass, and Bermuda grass

Petitioner's Response to Deficiency 3b

By limiting grass residue research to Bermuda grass, bluegrass, and fescue or bromegrass, areas such as southern Arizona, southern New Mexico, and west Texas (areas of current use and potential for tebuthiuron) would not qualify as site potentials since these grasses are not present.

In the proposed protocol, grass species native to the local area will be selected with preference given to bluegrass, Bermuda grass, and fescue or bromegrass. Each of these species will be represented in at least one (1) of the proposed eight (8) test locations. Other test locations, however, could utilize one of the major grass species in the area such as little bluestem, sideoats grama, buffalograss, etc.

DEB's Discussion/Conclusion re: Deficiency 3b

DEB has no objections to the petitioner's choice of grass species. We refer his attention, however, to the three maps provided on page 10 of this review.

Deficiencies 3c(1) through 3c(4)

Deficiency 3c(1)

Spike 20P is labeled for rangeland and pastureland applications whereas SPIKE 40P is labeled for pastureland applications only. The submitted protocol proposed application of Spike 40P to both rangeland and pastureland.

Petitioner's Response to Deficiency 3c(1)

The petitioner indicates that of the eight proposed testing sites, four will be on rangeland and four will be on pastureland. Spike 20P is registered for both rangeland and pastureland. Spike 40P is registered for pastureland only. Elanco proposes use of the 20P formulation on the four rangeland sites and the 40P formulation on the four pastureland sites.

DEB's Conclusion re: Deficiency 3c(1)

DEB has no objection to use of Spike 20P on the rangeland sites and Spike 40P on the pastureland sites. The test sites should involve at least 16 States.

Deficiency 3c(2)

The submitted protocols reflected ground application only. Unless the current labels (see DEB's Conclusion 2b above) are amended to restrict use to ground application only then the resubmitted protocols must be revised to reflect both ground and aerial applications.

Petitioner's Response to 3c(2)

See the response to Deficiency 2b.

DEB's Conclusion re: Deficiency 3c(2)

Deficiency 3c(2) is not resolved. Refer to the Conclusion re: Deficiency 2b.

Deficiency 3c(3)

The submitted protocols reflected broadcast application of the Spike 40P formulation. Unless the current label restriction (see DEB's Conclusion 2d above) against broadcast application of Spike 40P to pastureland is deleted by the registrant then the resubmitted protocol should reflect both broadcast and spot treatments to pastureland with both treatments at the maximum permissible label rates; if the label restriction is retained by the registrant then only spot treatments need be conducted on pastureland.

Petitioner's Response to Deficiency 3c(3)

The petitioner will revise the label so that Spike 40P can be applied broadcast and as single plant treatment. (Refer to Deficiency 2d.) However, the petitioner intends to make broadcast treatments, not individual plant treatments, to obtain the necessary residue data. The maximum label rate for broadcast applications is 4 lb ai/A. The petitioner calculates that the individual plant treatment rate is approximately 6 lb ai/A in a 45-foot square area around the base of the plant. However, single treatments would not be practical for more than 200 plants/A. Accordingly, the single plant treatment rate for 200 plants/A would be 1.5 lb ai/A on a broadcast basis. Therefore, the petitioner plans to conduct the residue trials at the rate of 4 lb ai/A, the maximum broadcast rate.

DEB's Conclusion re: Deficiency 3c(3)

DEB has no objection to use of the 4 lb ai/A rate for broadcast treatments provided the Spike 40P label is revised

so that the maximum broadcast rate for pastureland/rangeland is 4 lb ai/A.

A limited number of individual plant treatments are needed, however, unless the individual plant treatment directions are removed from the label.

Deficiency 3c(4)

The proposed application rate of 2.0 lb ai/A of SPIKE 40P in the registrant's Western Region protocol is inconsistent with the currently approved Spike 20P label. The latter label now recommends 3.0 lb ai/A for rangeland brush control in the Western United States. The resubmitted protocol should reflect Spike 20P applications in the Western Region at both 4.0 and 3.0 lb ai/A.

Petitioner's Response to Deficiency 3c(4)

The petitioner intends to make all applications at 4 lb ai/A.

DEB's Conclusion re: Deficiency 3c(4)

If the maximum rate for residue studies is to be 4 lb ai/A, the Spike 40P label must be revised so that the maximum application rate for pastureland and rangeland is 4 lb ai/A. The current Spike 40P label (submitted to EPA in February 1988) allows up to 15 lb Spike 40P/A (6 lb ai/A).

DEB concludes that deficiency 3c(4) regarding application rates for the residue studies is not resolved. The petitioner's residue data in Section D must support the intent of his label in Section B.

Other Considerations

A. Grazing/Haying Restrictions

In an early review for tebuthiuron residues in milk resulting from application of Graslan 20P at rates up to 20 lb/A (PP#2F2727, Al Smith, December 22, 1982), DEB stated the following:

> " . . . there is generally a 1-year deferred grazing period practiced. Moreover, this practice extends to the cutting for hay also. Nevertheless, some grazing and/or cutting for hay could occur.

> We believe that a 1-year restriction on the cutting of forage grass for hay is necessary and practical. Under this restriction, residues in hay would be less than 20 ppm. The ingestion of hay containing such levels by dairy cattle would result in milk residues of less than 0.3 ppm."

The Spike 20P label contains the statement: "Grazing is only allowed in areas treated with 20 lb/A or less of Spike 20P. In areas treated with 20 lb/A or less of Spike 20P, grass may be cut for hay one year after application."

The Spike 40P label contains the statements: "Grazing is allowed in areas treated with 10 lb/A or less of Spike 40P. In areas treated with 10 lb/A or less of Spike 40P, grass may be cut for hay one year after application."

DEB concludes that the following sentence should be added to both labels between the two sentences quoted above:

> "However, do not graze livestock within 1 year of application."

B. Frequency of Forage Sampling

The Registration Standard indicates that forage should be sampled every 2 weeks for the first 3 months after application and then monthly for 21 months. However, the petitioner indicates that initial sampling should be delayed until rain dissolves some of the pellet. The petitioner also indicates that sampling is not necessary during dormancy due to cold or drought.

The petitioner suggests that initial sampling be delayed until at least 0.5 inch of rain has fallen. The petitioner also suggests that sampling be suspended during dormancy.

The Registration Standard gives a broad outline as to what the testing schedule should achieve. The petitioner will need to adjust his sampling schedule with the testing area. For example, grasses grown in the southern States would not be subjected to as much cold weather as grasses grown in the northern States. Also, pasture irrigation is not uncommon in North America. We want to know the maximum residue level that may occur at any time following application.

C. Frequency of Hay Sampling

The Registration Standard indicates that hay should be sampled for 2 years after application. The petitioner indicates, however, that the Spike 20P and 40P labels have a 1-year restriction on cutting of hay from treated areas.

The petitioner proposes that hay sampling begin 1 year after application. Samples would be collected 2 to 4 times (as often as hay would normally be cut). Sampling would end approximately 2 years after application.

DEB has no objection to the petitioner's proposed sampling schedule for hay since there is a 1-year restriction on cutting of hay from treated areas.

D. Test Site - Natural or Artificial Brush/Grasses

DEB indicated that natural/existing rangeland/pastureland sites should be used.

E. Test Site Irrigation

DEB does not want areas to be irrigated which would not normally be irrigated. However, irrigated pastures are common in much of the United States.

F. Metabolites to be Assayed

DEB indicated that tebuthiuron per se and metabolites 103(OH), 104, and 109 are now considered to be the residues of concern. However, DEB has deferred to TB (in the Residue Chemistry Chapter dated February 27, 1987 of the Tebuthiuron Registration Standard) concerning the toxicological significance of the minor metabolites 104(OH), 106, 107, and 108. Each of the metabolites 104(OH), 106, 107, and 108 are expected to consist of only 1 to 2.4 percent of the terminal residue.

DEB also suggested that the petitioner keep frozen samples in case analysis of additional metabolites is later found to be necessary.

cc: N.Dodd (DEB), M.Kovacs, TOX, Registration Standard File (Tebuthiuron), RF, SF (Tebuthiuron), Circulation (6), E.Eldredge (ISB/PMSD)

RDI:J.Onley:1/17/89:RDSchmitt:1/30/89
TS-769:DEB:CM#2:Rm80D:X1681:Edited by fmm 2/8/89